UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/942,075	08/28/2001	George Treacy	0148.1135-010	6161

21005 7590 08/21/2003

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.
530 VIRGINIA ROAD
P.O. BOX 9133
CONCORD, MA 01742-9133

EXAMINER	
NOLAN, PATRICK J	
ART UNIT	**PAPER NUMBER**
1644	5

DATE MAILED: 08/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/942,075	TREACY, GEORGE	
	Examiner	Art Unit	
	Patrick J. Nolan	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-12 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-12 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. Claims 1-12 are pending. Applicant is requested to update the status of all related applications in the specification, particularly on page 1.

2. Claims 3-4, 7-8 and 11-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3-4, 7-8 and 11-12 are indefinite in the recitation of monoclonal antibody cA2 because its characteristics are not known. The use of cA2 monoclonal antibody as the sole means of identifying the claimed antibody renders the claim indefinite because "cA2" is merely a laboratory designation which does not clearly define the claimed product, since different laboratories may use the same laboratory designations to define completely distinct monoclonal antibodies. Amendment of the claims to include the ATCC or depository number would obviate this rejection.

3. Claims 3-4, 7-8 and 11-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The monoclonal antibody cA2 recited in claims 3-4, 7-8 and 11-12 are essential to the claimed invention. The reproduction of monoclonal antibodies is an unpredictable event. The cA2 monoclonal antibodies and the cell line c168A which produces the cA2 monoclonal antibody, disclosed on page 7 of the specification, must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The instant specification does not disclose a repeatable process to obtain the monoclonal antibody or cell line, and it is not apparent if the monoclonal antibody is readily available to the public. If the deposits have been made under the terms of the Budapest Treaty, an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the monoclonal antibody producing hybridoma or cell line have been deposited under the Budapest Treaty and that the monoclonal antibody will be irrevocably and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808. Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of deposit or 5 years after the last request for a sample **or for the enforceable life of the patent whichever is longer.** See 37 CFR 1.806. If the deposit has not been made under the Budapest treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature must be made, stating that the deposit has been made at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809, have been met.

Amendment of the specification to disclose the date of deposit and the complete name and address of the depository is required.

If the deposit was made after the effective filing date of the application for a patent in the United States, a verified statement is required from a person in a position to corroborate that the

plasmid described in the specification as filed are the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicant's possession at the time the application was filed.

Applicant's attention is directed to *In re Lundak*, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985), and 37 CFR 1.801-1.809 for further information concerning deposit practice.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claim 5 is rejected under 35 U.S.C. § 102(b) as being anticipated by Konno et al. (AV).

Konno et al., teaches a method of treating an individual mouse (i.e. individual is interpreted broadly as to encompass an individual organism) by the administration of a therapeutically effective amount of an anti-TNF- antibody (see Table 3, in particular). It is noted that by decreasing air overflow in rats made airway hyperresponsive by the administration of LPS, the prior art teaches treatment of airway inflammation.

The prior art teachings anticipate the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

5. Claim 1 is rejected under 35 U.S.C. § 103 as being unpatentable over Konno et al. (AV) in view of Shah et al. (AY).

Konno et al., has been discussed supra.

The claimed invention differs from the prior art teaching(s) by the recitation of treating asthma with an anti-TNF- antibody. However, Konno et al., teaches that LPS components of gram-negative bacteria are known to be one of important stimuli in the development of asthma (page 315, 1st column, in particular). Furthermore, Konno et al., teaches that airway hyperresponsiveness is a characteristic feature of bronchial asthma. Shah et al., teaches that TNF- is an important mediator of asthma and that patients with symptomatic asthma had 20 times greater amounts of TNF- in their lung fluid then asymptomatic patients (page 1039, 2nd column, in particular). Shah et al., also teaches that an anti-TNF- monoclonal antibody had exciting and dramatic beneficial results in treating rheumatoid arthritis and since TNF- plays a fundamental role in both the inflammation and acquired bronchial hyperresponsiveness it raises possible new therapeutic intervention in the treatment of asthma (page 1042, in particular).

One of ordinary skill in the art at the time the invention was made would have been motivated to treat asthma with the anti-TNF- antibody taught by Konno et al., because the anti-TNF- antibody taught by Konno et al., was effective in reducing airway hyperresponsiveness in LPS treated mice and airway hyperresponsiveness is a characteristics feature of bronchial asthma, as taught by Konno et al., and because Shah et al., teaches TNF- is an important mediator of asthma and that patients with symptomatic asthma had 20 times greater amounts of TNF- in their lung fluid then asymptomatic patients and that an anti-TNF- monoclonal antibody had exciting and dramatic beneficial results in treating rheumatoid arthritis and that since TNF- plays a fundamental role in both the inflammation and acquired bronchial hyperresponsiveness it raises possible new therapeutic intervention in the treatment of asthma. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

6. Claims 2 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Konno et al., in view of Shah et al., as applied to claims 1 and 5 above, and further in view of U.S. Patent 5,698,195 (AA).

Konno et al., and Shah et al., have been discussed supra. The claimed invention differs from the prior art teachings by the recitations of using a chimeric antibody in a method of treating airway inflammation or asthma.

However, the '195 patent teaches how to make chimeric antibodies (columns 10 and 19-20, in particular). The '195 patent also teaches the use of chimeric antibodies over antibodies derived from a single non-human species because they reduce the immunogenecity of the antibody in application and allow for increased yields (column 10, in particular).

One of ordinary skill in the art at the time the invention was made would have been motivated to treat asthma and/or airway inflammation with the anti-TNF- antibody taught by the combined teachings of Konno et al., and Shah et al., and make the antibody a chimeric antibody as taught by the '195 patent because the use of chimeric antibodies over antibodies derived from a single non-human species reduce the immunogenecity of the antibody in application and allow for increased yields. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed

invention. Therefore, the invention as a whole is prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

7. Claims 1-12 are rejected under 35 U.S.C. § 103 as being unpatentable over U.S. Patent 5,698,195 (AA), in view of Shah et al. (AY) and Lukacs et al. (AS).

The '195 patent teaches a chimeric antibody cA2, which has high affinity, epitope specificity and the ability to neutralize the cytotoxic effects of human TNF- (column 20, in particular). The '195 patent also teaches the use of a therapeutically effective amount of the cA2 antibody in treating a subject (i.e. an individual) having a pathology associated with abnormal levels of TNF- , when compared with the levels of TNF- in a normal healthy subject (columns 34-35 and 56-75, in particular).

The claimed invention differs from the prior art teachings by the recitation of treating asthma and/or airway inflammation and/or asthma associated lung inflammatory cell accumulation with the cA2 anti-TNF- antibody. It is noted that asthma is a form of airway inflammation, as taught by Shah et al., (page 1038, 1st column, in particular), so a method of treating asthma, would also treat airway inflammation. Shah et al., also teaches that TNF- is an important mediator of asthma and that patients with symptomatic asthma had 20 times greater amounts of TNF- in their lung fluid then asymptomatic patients (page 1039, 2nd column, in particular). In addition Shah et al., also teaches that their is increased levels of TNF- in the sputum of patients with acute attacks of asthma, and that mRNA levels of TNF- in the cells of the lungs of asthmatic subjects were increased when compared to normal unaffected people (page 1039, in particular). Furthermore, Shah et al., also teaches that an anti-TNF- monoclonal antibody had exciting and dramatic beneficial results in treating rheumatoid arthritis and since TNF- plays a fundamental role in both the inflammation and acquired bronchial hyperresponsiveness it raises possible new therapeutic intervention in the treatment of asthma (page 1042, in particular). Lastly, Lukacs et al., teaches that TNF- mediates the recruitment (i.e. accumulation) of neutrophils and eosinophils during airway inflammation.

One of ordinary skill in the art at the time the invention was made would have been motivated to use a therapeutically effective amount of the cA2 anti-TNF- chimeric antibody taught by the '195 patent in a method of treatment of asthma and/or airway inflammation and/or asthma associated lung inflammatory cell accumulation because the '195 patent teaches the use of a therapeutically effective amount of the cA2 antibody in treating a subject (i.e. an individual) having a pathology associated with abnormal levels of TNF- , when compared with the levels of TNF- in a normal healthy subject and Shah et al., teaches that (1) TNF- is an important mediator of asthma, (2) patients with symptomatic asthma had 20 times greater amounts of TNF- in their lung fluid then asymptomatic patients, (3) their are increased levels of TNF- in the sputum of patients with acute attacks of asthma, and that mRNA levels of TNF- in the cells of the lungs of asthmatic subjects were increased when compared to normal unaffected people, (4) and since an anti-TNF- monoclonal antibody had exciting and dramatic beneficial results in treating rheumatoid arthritis and since TNF- plays a fundamental role in both the inflammation and acquired bronchial hyperresponsiveness it raises possible new therapeutic intervention in the treatment of asthma (page 1042, in particular) and (5) Lukacs et al., teaches that TNF- mediates the recruitment (i.e. accumulation) of neutrophils and eosinophils during airway inflammation . From the teachings of the references, it is apparent that one of ordinary skill in the art would

have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

8. Applicant is notified that page 2 of the IDS filed 1-18-02 has not matched with the file. Applicant is requested to refurnish said page.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick Nolan whose telephone number is (703) 305-1987. The examiner can normally be reached on Monday through Friday from 8:30 am to 4:30 pm.

10. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Christina Chan, can be reached at (703) 305-3973. The FAX number for our group, 1644, is (703) 872-9306. Any inquiry of a general nature relating to the status of this application or proceeding should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Patrick J. Nolan, Ph.D.
Patent Examiner, Group 1640
8/20/03